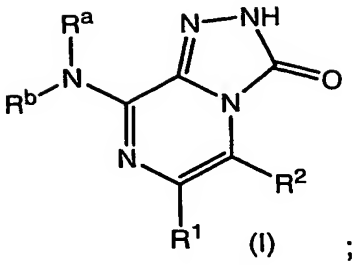
CLAIMS

1. A compound of formula (I)



(I) ;

the prodrugs thereof, and the pharmaceutically acceptable salts of the compounds and prodrugs, wherein:

R^a and R^b are, independently:

(1) hydrogen;

(2) acetyl;

(3) -(C_1-C_6)alkyl, optionally, and independently, substituted with from one to three:

(A) cyano; (B) halogen; (C) -NR^3R^4; (D) -COR^5; (E) -OR^6; (F) -SR^6; (G) -$S(O)R^6$; (H) -SO_2R^6; (I) aryl, optionally substituted independently with from one to three halogen; nitro; -SO_2NH_2; -(C_1-C_6)alkyl; methylenedioxy; -COR^5; or -OR^6; (J) heteroaryl, optionally substituted independently with from one to three hydroxy; nitro; halogen; -OR^6; aryl, optionally substituted independently with -(C_1-C_6)alkyl; heteroaryl; trifluoromethyl; or -(C_1-C_6)alkyl, optionally substituted with hydroxy; (K) -(C_3-C_{11})cycloalkyl, optionally substituted independently with from one to three cyano; -COR^5; or -$CH_2NR^3R^4$; or (L) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three -(C_1-C_6)alkyl, optionally substituted with aryl; -COR^5; aryl, optionally substituted independently with halogen; oxo; or -(C_1-C_6)alkoxy; wherein:

R^3 and R^4 are independently:

(a) hydrogen; (b) -SO_2R^6; (c) aryl, optionally substituted independently with from one to three halogen; cyano; nitro; -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, or -COR^5; (d) -(C_1-C_6)alkyl, optionally substituted independently with from one to three -(C_3-C_{11})heterocycloalkyl; -(C_3-C_{11})cycloalkyl; -(C_1-C_6)alkoxy; aryl; or heteroaryl; (e) heteroaryl, optionally substituted independently with from one to three halogen; trifluoromethyl; cyano; nitro; -COR^5; -(C_1-C_6)alkyl, optionally substituted with -(C_3-

C_{11})heterocycloalkyl; or -(C_1-C_6)alkoxy; (f) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three -(C_1-C_6)alkyl; or (g) -COR^5; or

R^3 and R^4, taken together with the nitrogen atom to which they are attached, form a 5- or 6-membered heterocycloalkyl ring, optionally having from one to three additional heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein said 5- or 6-membered heterocycloalkyl ring is optionally substituted independently with from one to three -(C_1-C_6)alkyl, optionally substituted with aryl;

R^5 is (h) hydroxy; (i) -(C_1-C_6)alkyl, optionally substituted independently with from one to three -CO_2H; -(C_1-C_6)alkoxy; or aryl; (j) -(C_1-C_6)alkoxy; (k) aryl, optionally substituted with halogen; (l) heteroaryl; or (m) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three oxo; -CO_2H; or -(C_1-C_6)alkyl; and

R^6 is (n) hydrogen; (o) -(C_1-C_6)alkyl, optionally substituted independently with from one to three hydroxy; -(C_1-C_6)alkoxy; aryl, optionally substituted with halogen; or heteroaryl, optionally substituted with -$CH_2NR^3R^4$; (p) aryl, optionally substituted independently with from one to three halogen; -(C_1-C_6)alkyl; cyano; trifluoromethyl; or -OR^6; (q) heteroaryl, optionally substituted independently with from one to three amino; -(C_1-C_6)alkyl; -(C_1-C_6)alkoxy; or -COR^5; or (r) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three -(C_1-C_6)alkyl;

(4) -(C_3-C_{11})cycloalkyl; or

(5) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three halogen; -COR^5; -(C_1-C_6)alkyl; or -(C_1-C_6)alkoxy; or

R^a and R^b, taken together with the nitrogen atom to which they are attached, form a 5- or 6-membered heterocycloalkyl ring, optionally having from one to three additional heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur, wherein said 5- or 6-membered heterocycloalkyl ring is optionally, and independently, substituted with from one to three halogen; -(C_1-C_6)alkyl; or heteroaryl, optionally substituted independently with from one to three halogen; trifluoromethyl; and cyano; and

R^1 and R^2 are, independently, (ii) hydrogen; (iii) halogen; (iv) aryl, optionally substituted independently with from one to three halogen; cyano; -(C_1-C_6)alkyl; -(C_1-C_6)alkoxy; -COR^5; or -$CONR^3R^4$; (v) -(C_1-C_6)alkyl, optionally substituted independently with from one to three aryl, optionally substituted independently with from one to three halogen or trifluoromethyl; heteroaryl; -$CONR^3R^4$; or hydroxy; (vi) -

COR^5; (vii) $-CONR^3R^4$; or (viii) $-(C_1-C_6)$cycloalkyl, optionally substituted independently with from one to three $-COR^5$.

2. A compound of claim 1, wherein:

R^a and R^b are, independently:

(1) hydrogen;

(3) $-(C_1-C_6)$alkyl, optionally, and independently, substituted with from one to three:

(A) cyano; (B) halogen; (C) $-NR^3R^4$; (D) $-COR^5$; (E) $-OR^6$; (F) $-SR^6$; (G) $-S(O)R^6$; (H) $-SO_2R^6$; (I) aryl, optionally substituted independently with from one to three halogen; nitro; $-SO_2NH_2$; $-(C_1-C_6)$alkyl; methylenedioxy; $-COR^5$; or $-OR^6$; (J) heteroaryl, optionally substituted independently with from one to three hydroxy; nitro; halogen; $-OR^6$; aryl, optionally substituted independently with $-(C_1-C_6)$alkyl; heteroaryl; trifluoromethyl; or $-(C_1-C_6)$alkyl, optionally substituted with hydroxy; (K) $-(C_3-C_{11})$cycloalkyl, optionally substituted independently with from one to three cyano; $-COR^5$; or $-CH_2NR^3R^4$; or (L) $-(C_3-C_{11})$heterocycloalkyl, optionally substituted independently with from one to three $-(C_1-C_6)$alkyl, optionally substituted with aryl; $-COR^5$; aryl, optionally substituted independently with halogen; oxo; or $-(C_1-C_6)$alkoxy; wherein:

R^3 and R^4 are independently:

(a) hydrogen; (b) $-SO_2R^6$; (c) aryl, optionally substituted independently with from one to three halogen; cyano; nitro; $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkoxy, or $-COR^5$; (d) $-(C_1-C_6)$alkyl, optionally substituted independently with from one to three $-(C_3-C_{11})$heterocycloalkyl; $-(C_3-C_{11})$cycloalkyl; $-(C_1-C_6)$alkoxy; aryl; or heteroaryl; (e) heteroaryl, optionally substituted independently with from one to three halogen; trifluoromethyl; cyano; nitro; $-COR^5$; $-(C_1-C_6)$alkyl, optionally substituted with $-(C_3-C_{11})$heterocycloalkyl; or $-(C_1-C_6)$alkoxy; (f) $-(C_3-C_{11})$heterocycloalkyl, optionally substituted independently with from one to three $-(C_1-C_6)$alkyl; or (g) $-COR^5$; or

R^3 and R^4, taken together with the nitrogen atom to which they are attached, form a 5- or 6-membered heterocycloalkyl ring, optionally having from one to three additional heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein said 5- or 6-membered heterocycloalkyl ring is optionally substituted with from one to three $-(C_1-C_6)$alkyl, optionally substituted with aryl;

R^5 is (h) hydroxy; (i) -(C_1-C_6)alkyl, optionally substituted independently with from one to three -CO_2H; -(C_1-C_6)alkoxy; or aryl; (j) -(C_1-C_6)alkoxy; (k) aryl, optionally substituted with halogen; (l) heteroaryl; or (m) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three oxo; -CO_2H; or -(C_1-C_6)alkyl; and

R^6 is (n) hydrogen; (o) -(C_1-C_6)alkyl, optionally substituted independently with from one to three hydroxy; -(C_1-C_6)alkoxy; aryl, optionally substituted with halogen; or heteroaryl, optionally substituted with -$CH_2NR^3R^4$; (p) aryl, optionally substituted independently with from one to three halogen; -(C_1-C_6)alkyl; cyano; trifluoromethyl; or -OR^6; (q) heteroaryl, optionally substituted independently with from one to three amino; -(C_1-C_6)alkyl; -(C_1-C_6)alkoxy; or -COR^5; or (r) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three -(C_1-C_6)alkyl;

(4) -(C_3-C_{11})cycloalkyl; or

(5) -(C_3-C_{11})heterocycloalkyl, optionally substituted independently with from one to three halogen; -COR^5; -(C_1-C_6)alkyl; or -(C_1-C_6)alkoxy; and

R^1 and R^2 are, independently, (ii) hydrogen; (iv) aryl, optionally substituted independently with from one to three halogen; cyano; -(C_1-C_6)alkyl; -(C_1-C_6)alkoxy; -COR^5; or -$CONR^3R^4$; or (v) -(C_1-C_6)alkyl, optionally substituted independently with from one to three aryl, optionally substituted independently with from one to three halogen or trifluoromethyl; heteroaryl; -$CONR^3R^4$; or hydroxy.

3. A compound of claim 1, wherein:

R^a and R^b are, independently:

(1) hydrogen;

(3) -(C_1-C_6)alkyl, optionally, and independently, substituted with one or two:

(A) cyano; (E) -OR^6; (F) -SR^6; (I) aryl, optionally substituted with nitro; (J) heteroaryl, optionally substituted independently with one or two -OR^6 or -(C_1-C_6)alkyl; or (L) -(C_3-C_{11})heterocycloalkyl, optionally substituted with oxo or -COR^5; wherein R^6 is (n) hydrogen; (o) -(C_1-C_6)alkyl; (p) aryl, optionally substituted with cyano or -OR^6; or (q) heteroaryl, optionally substituted with amino; -(C_1-C_6)alkyl; -(C_1-C_6)alkoxy; or -COR^5;

(4) -(C_3-C_{11})cycloalkyl; or

(5) -(C_3-C_{11})heterocycloalkyl, optionally substituted with -COR^5; wherein R^5 is (h) hydroxy; (i) -(C_1-C_6)alkyl; or (j) -(C_1-C_6)alkoxy; and

R^1 and R^2 are, independently, hydrogen or -(C_1-C_6)alkyl.

4. A compound of claim 1 selected from the group consisting of:

5-[2-(6-*tert*-butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-nicotinic acid methyl ester;

8-[2-(3-aminopyridin-2-yloxy)-ethylamino]-6-*tert*-butyl-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

3-(6-*tert*-butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-propionitrile;

4-(6-*tert*-butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-piperidine-1-carboxylic acid ethyl ester;

3-[2-(6-*tert*-butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-ethoxy]-benzonitrile;

8-[2-(benzothiazol-2-ylamino)-ethylamino]-6-*tert*-butyl-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(4-methoxy-phenoxy)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(7-methyl-1H-benzoimidazol-2-yl)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(pyridin-3-yloxy)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(pyridin-4-yloxy)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[3-(3,5-dimethyl-pyrazol-1-yl)-propylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(3-imidazol-1-yl-propylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(3-morpholin-4-yl-propylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[3-(2-oxo-pyrrolidin-1-yl)-propylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[(pyridin-3-ylmethyl)-amino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[(pyridin-4-ylmethyl)-amino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[(tetrahydro-furan-2-yl-methyl)-amino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(2-ethylsulfanyl-ethylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(2-hydroxy-1-methyl-ethylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(6-hydroxy-hexylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(2-methoxy-ethylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(2-pyridin-3-yl-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(2-pyridin-4-yl-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(4-nitro-benzylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

4-(6-*tert*-butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-piperidine-1-carboxylic acid ethyl ester;

6-*tert*-butyl-8-[2-(2-methyl-pyridin-3-yloxy)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(2-methyl-pyridin-3-yl)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(6-methoxy-pyridin-3-yl)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-[2-(6-methyl-pyridin-3-yl)-ethylamino]-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-*tert*-butyl-8-(3-methoxy-propylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

6-isopropyl-5-methyl-8-(2-pyridin-3-yl-ethylamino)-2H-[1,2,4]triazolo[4,3-a]pyrazin-3-one;

a prodrug thereof, or a pharmaceutically acceptable salt of said compound or said prodrug.

5. A pharmaceutical composition comprising an amount of a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or prodrug; and a pharmaceutically acceptable carrier, vehicle, or diluent.

6. A method of treating a glycogen synthase kinase 3-mediated condition, disease, or symptom in a mammal in need of such treatment which method comprises administering to said mammal a therapeutically effective amount of a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or prodrug; or a pharmaceutical composition comprising said compound of claim 1, or said prodrug thereof, or said pharmaceutically acceptable salt of said compound or prodrug.

7. A method of claim 6, wherein said condition, disease, or symptom is Alzheimer's Disease, asthma, atherosclerosis, anxiety, bipolar disorder, cancer, diabetes, dementia, depression, frailty, hair loss, heart failure, essential hypertension, hyperglycemia, hyperlipidemia, hypoglycemia, inflammation, ischemia, male fertility and sperm motility, mood disorders, neuronal cell death, obesity, obsessive compulsive disorder, polycystic ovary disorder, schizophrenia, stroke, Syndrome X, or traumatic brain injury.

8. A method of inhibiting glycogen synthase kinase-3 activity in a mammal in need of such inhibition which method comprises administering to said mammal a glycogen synthase kinase-3 inhibiting amount of a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or prodrug; or a pharmaceutical composition comprising said compound of claim 1, or said prodrug thereof, or said pharmaceutically acceptable salt of said compound or prodrug.

9. A pharmaceutical composition comprising:

(a) an amount of a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or prodrug;

(b) an amount of one or more of: (i) an anti-angiogenesis agent, (ii) a signal transduction inhibitor, (iii) an anti-proliferative agent, (iv) an NK-1 receptor antagonist, (v) a $5HT_{1D}$ receptor antagonist, (vi) a selective serotonin reuptake inhibitor, (vii) an anti-psychotic agent, (viii) an acetylcholinesterase inhibitor, (ix) a neuroprotectant, (x) tissue plasminogen activator, (xi) neutrophil inhibitory factor, or (xii) a potassium channel modulator; and

(c) a pharmaceutically acceptable carrier, vehicle, or diluent.

10. A composition of claim 9, wherein: (i) said anti-angiogenesis agent is celecoxib, valdecoxib, or rofecoxib; (ii) said signal transduction inhibitor is an epidermal growth factor receptor response inhibitor, a vascular endothelial growth factor inhibitor, or an erbB2 receptor inhibitor; (vi) said selective serotonin reuptake inhibitor is fluoxetine, paroxetine, sertraline, fluvoxamine, venlafaxine, nefazodone, or bupropion; (vii) said anti-psychotic agent is ziprasidone, olanzapine, risperidone, sonepiprazole, or gepirone; (viii) said acetylcholinesterase inhibitor is donepezil, rivastigmine, metrifonate, physostigmine, or tacrine; and (ix) said neuroprotectant is an NMDA receptor antagonist.

11. A method of treating a glycogen synthase kinase 3-mediated condition, disease, or symptom in a mammal in need of such treatment which method comprises administering to said mammal a therapeutically effective amount of a composition of claim 9.

12. A method of claim 11, wherein said condition, disease, or symptom is Alzheimer's Disease, asthma, atherosclerosis, anxiety, bipolar disorder, cancer, diabetes, dementia, depression, frailty, hair loss, heart failure, essential hypertension, hyperglycemia, hyperlipidemia, hypoglycemia, inflammation, ischemia, male fertility and sperm motility, mood disorders, neuronal cell death, obesity, obsessive compulsive disorder, polycystic ovary disorder, schizophrenia, stroke, Syndrome X, or traumatic brain injury.